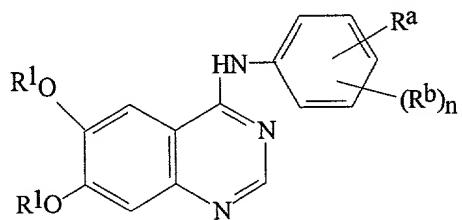


WE CLAIM:

1. A formulation comprising:

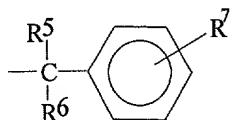
5 (a) a phospholipid; and

(b) a quinazoline compound of the formula:



wherein:

10 R^a is hydrogen, halo, hydroxy, mercapto, (C₁-C₄)hydroxyalkyl, methylenedioxy, ethylenedioxy, benzyloxy, OCF₃, SCF₃, SO₃H, SO₂F, SO₂NR²R³ in which R² is hydrogen or (C₁-C₄)alkyl and R³ is hydrogen, (C₁-C₄)alkyl, or phenyl, NR²R⁴ in which R² is as defined above and R⁴ is phenyl, or R^a a group of the formula:



15 in which R⁵ and R⁶ are each, independently, hydrogen, (C₁-C₄)alkyl, or (C₁-C₄)perfluoroalkyl, and R⁷ is hydrogen, halo, hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)hydroxyalkyl, or N(R²)₂ in which R² is as defined above;

n is an integer of 1-4;

20 R^b is each, independently, hydrogen, halo, hydroxy, mercapto, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)thioalkyl, (C₁-C₄)hydroxyalkyl, nitro, cyano, methylenedioxy, ethylenedioxy, COCH₃, CF₃, OCF₃, SCF₃, COOH, SO₃H, SO₂F, phenyl or phenyl substituted by a group selected from halo, hydroxy, mercapto, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)thioalkyl, (C₁-C₄)hydroxyalkyl,

amino, nitro, cyano, CF_3 , COOH , SO_3H , $\text{SO}_2\text{NR}^2\text{R}^3$ in which R^2 and R^3 are as defined below, and SO_2F ;

5 R^a is also benzyloxy substituted on the phenyl portion by a group defined above, NR^2R^3 in which R^2 is H or $(\text{C}_1\text{-C}_4)\text{alkyl}$ and R^3 is H, $(\text{C}_1\text{-C}_4)\text{alkyl}$, phenyl or phenyl substituted by a group as defined above;

R^1 is $(\text{C}_1\text{-C}_4)\text{alkyl}$, or a pharmaceutically acceptable salt thereof.

2. The formulation of claim 1, wherein the quinazoline compound is an acid addition salt.

10

3. The formulation of claim 1, wherein R^1 is methyl.

4. The formulation of claim 1, wherein the quinazoline compound is selected from:

15 4-(3',5'-dibromo-4'-methylphenyl)amino-6,7-dimethoxyquinazoline,

4-(2',4',6'-tribromophenyl)amino-6,7-dimethoxyquinazoline,

15 4-(2',3',5',6'-tetrafluoro-4'-bromophenyl)amino-6,7-dimethoxyquinazoline,

4-(4'-fluorophenyl)amino-6,7-dimethoxyquinazoline,

4-(3'-fluorophenyl)amino-6,7-dimethoxyquinazoline,

4-(2'-fluorophenyl)amino-6,7-dimethoxyquinazoline,

20 4-(4'-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,

4-(2'-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,

4-(3',5'-bis-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,

4-(3',5'-dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline, and

4-(3'-chloro-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline.

25

5. The formulation of claim 1, wherein the quinazoline compound is selected from:

4-(3',5'-dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,

4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,

4-(3'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,
4-(2'-hydroxy-naphthyl-3')-amino-6,7-dimethoxyquinazoline,
4-{4'-[2''-(4''-aminophenyl)-hexafluoropropyl]phenyl}-amino-6,7-
dimethoxyquinazoline, and
5 4-(3'-trifluoromethoxylphenyl)-amino-6,7-dimethoxyquinazoline.

6. The formulation of claim 1, wherein the phospholipid is an unsaturated phospholipid.

10 7. The formulation of claim 1, wherein the phospholipid is an anionic phospholipid.

8. The formulation of claim 1, wherein the phospholipid is a polyethylene glycol phospholipid.

15 9. The formulation of claim 1, wherein the phospholipid is a polyethylene glycol phosphatidylethanolamine.

10. The formulation of claim 1, wherein the phospholipid is 1,2-dipalmitoyl-sn-
20 glycero-3-phosphoethanolamine-N-[poly(ethylene glycol)5000].

11. The formulation of claim 1, wherein the phospholipid is 1,2-dipalmitoyl-sn-
glycero-3-phosphoethanolamine-N-[poly(ethylene glycol)2000].

25 12. The formulation of claim 1, further comprising a surfactant.

13. The formulation of claim 11, wherein the surfactant is a block copolymer of ethyleneoxide and propyleneoxide.

14. The formulation of claim 1, further comprising propylene glycol.

15. The formulation of claim 1, further comprising:

5 (c) a surfactant
(d) propylene glycol and
(e) water.

16. The formulation of claim 15, wherein the phospholipid is polyethylene glycol
10 phosphatidylethanolamine and the surfactant is a block copolymer of ethyleneoxide and
propyleneoxide.

17. The formulation of claim 15, wherein the phospholipid is an anionic
phospholipid and the quinazoline compound is a cationic quinazoline compound.

15
18. The formulation of claim 15, wherein:
(a) the phospholipid concentration is about 0.2 to 2.5 w/v%;
(b) the quinazoline concentration is less than about 0.2 w/v%;
(c) the surfactant concentration is about 0.05-2 w/v%;
20 (d) the propylene glycol concentration is about 5-20 w/v%; and
(e) the balance is water.

19. The formulation of claim 18, wherein:

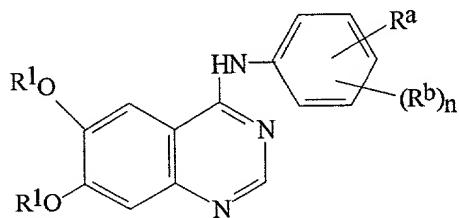
25 (a) the phospholipid concentration is about 1.84 w/v%;
(b) the quinazoline concentration is about 0.2 w/v%;
(c) the surfactant concentration is about 0.42 w/v%;
(d) the propylene glycol concentration is about 9.33 w/v%; and
(e) the water concentration is 88.21.

20. The formulation of claim 1, wherein the phospholipid and quinazoline compound form a micellar formulation with a mean particle size less than about 10 nm.

5 21. The formulation of claim 15, wherein the phospholipid and quinazoline compound form a micellar formulation with a mean particle size less than about 10 nm.

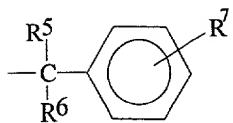
22. A formulation comprising:

- (a) a low hydrophylicity lipophylicity balance portion comprising:
 - (i) a block copolymer of ethylene oxide and propylene oxide;
 - (ii) an ethoxylated castor oil;
 - (iii) propylene glycol;
- (b) a high hydrophylicity lipophylicity balance portion comprising:
 - (i) lecithin;
 - (ii) a triglyceride of caprylic acid;
- (c) water; and
- (d) a quinazoline compound of the formula:



wherein:

20 R^a is hydrogen, halo, hydroxy, mercapto, (C₁-C₄)hydroxyalkyl, methylenedioxy, ethylenedioxy, benzyloxy, OCF₃, SCF₃, SO₃H, SO₂F, SO₂NR²R³ in which R² is hydrogen or (C₁-C₄)alkyl and R³ is hydrogen, (C₁-C₄)alkyl, or phenyl, NR²R⁴ in which R² is as defined above and R⁴ is phenyl, or R^a a group of the formula:



in which R⁵ and R⁶ are each, independently, hydrogen, (C₁-C₄)alkyl, or (C₁-C₄)perfluoroalkyl, and R⁷ is hydrogen, halo, hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)hydroxyalkyl, or N(R²)₂ in which R² is as defined above;

5 n is an integer of 1-4;

R^b is each, independently, hydrogen, halo, hydroxy, mercapto, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)thioalkyl, (C₁-C₄)hydroxyalkyl, nitro, cyano, methylenedioxy, ethylenedioxy, COCH₃, CF₃, OCF₃, SCF₃, COOH, SO₃H, SO₂F, phenyl or phenyl substituted by a group selected from halo, hydroxy, mercapto, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)thioalkyl, (C₁-C₄)hydroxyalkyl, 10 amino, nitro, cyano, CF₃, COOH, SO₃H, SO₂NR²R³ in which R² and R³ are as defined below, and SO₂F;

15 R^a is also benzyloxy substituted on the phenyl portion by a group defined above, NR²R³ in which R² is H or (C₁-C₄)alkyl and R³ is H, (C₁-C₄)alkyl, phenyl or phenyl substituted by a group as defined above;

R¹ is (C₁-C₄)alkyl, or a pharmaceutically acceptable salt thereof.

23. The formulation of claim 22, wherein the low hydrophylicity lipophylicity balance portion, the high hydrophylicity lipophylicity balance portion, the water and the 20 quinazoline compound form a microemulsion with a mean particle size of about 10-25 nm.

24. The formulation of claim 22, wherein the low hydrophylicity lipophylicity balance portion comprises:

25 (i) about 2 w/v% of the block copolymer of ethylene oxide and propylene oxide;

- (ii) about 18 w/v% of the ethoxylated castor oil; and
- (iii) about 80 w/v% of the propylene glycol.

25. The formulation of claim 22, wherein the high hydrophylicity lipophylicity
5 balance portion comprises:

- (i) about 40 w/v% of the lecithin; and
- (ii) about 60 w/v% of the triglyceride of caprylic acid.

26. The formulation of claim 22, wherein the low hydrophylicity lipophylicity
10 balance portion comprises:

- (i) about 2 w/v% of the block copolymer of ethylene oxide and
propylene oxide;
- (ii) about 18 w/v% of the ethoxylated castor oil;
- (iii) about 80 w/v% of the propylene glycol; and

15 the high hydrophylicity lipophylicity balance portion comprises:

- (i) about 40 w/v% of the lecithin;
- (ii) about 60 w/v% of the triglyceride of caprylic acid;

the water and the quinazoline compound form a microemulsion with a mean particle
size of about 10-25 nm.

20

27. The formulation of claim 22, wherein the quinazoline compound is an acid
addition salt.

28. The formulation of claim 22, wherein the quinazoline compound is selected
25 from:

- 4-(3',5'-dibromo-4'-methylphenyl)amino-6,7-dimethoxyquinazoline,
- 4-(2',4',6'-tribromophenyl)amino-6,7-dimethoxyquinazoline,
- 4-(2',3',5',6'-tetrafluoro-4'-bromophenyl)amino-6,7-dimethoxyquinazoline,

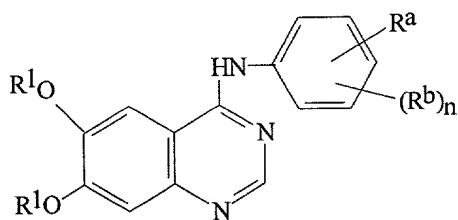
4-(4'-fluorophenyl)amino-6,7-dimethoxyquinazoline,
 4-(3'-fluorophenyl)amino-6,7-dimethoxyquinazoline,
 4-(2'-fluorophenyl)amino-6,7-dimethoxyquinazoline,
 4-(4'-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,
 5 4-(2'-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,
 4-(3',5'-bis-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,
 4-(3',5'-dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline, and
 4-(3'-chloro-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline.

10 29. The formulation of claim 22, wherein the quinazoline compound is selected from:

4-(3',5'-dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,
 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,
 4-(3'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,
 15 4-(2'-hydroxy-naphthyl-3')-amino-6,7-dimethoxyquinazoline,
 4-{4'-[2''-(4'''-aminophenyl)-hexafluoropropyl]phenyl}-amino-6,7-
 dimethoxyquinazoline, and
 4-(3'-trifluoromethoxyphenyl)-amino-6,7-dimethoxyquinazoline.

20 30. A method of making a formulation comprising:

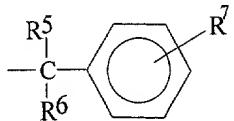
(a) providing a quinazoline compound of the formula:



wherein:

25 R^a is hydrogen, halo, hydroxy, mercapto, (C₁-C₄)hydroxyalkyl, methylenedioxy, ethylenedioxy, benzyloxy, OCF₃, SCF₃, SO₃H, SO₂F,

$\text{SO}_2\text{NR}^2\text{R}^3$ in which R^2 is hydrogen or $(\text{C}_1\text{-C}_4)\text{alkyl}$ and R^3 is hydrogen, $(\text{C}_1\text{-C}_4)\text{alkyl}$, or phenyl, NR^2R^4 in which R^2 is as defined above and R^4 is phenyl, or R^a a group of the formula:



5 in which R^5 and R^6 are each, independently, hydrogen, $(\text{C}_1\text{-C}_4)\text{alkyl}$, or $(\text{C}_1\text{-C}_4)\text{perfluoroalkyl}$, and R^7 is hydrogen, halo, hydroxy, $(\text{C}_1\text{-C}_4)\text{alkyl}$, $(\text{C}_1\text{-C}_4)\text{alkoxy}$, $(\text{C}_1\text{-C}_4)\text{hydroxyalkyl}$, or $\text{N}(\text{R}^2)_2$ in which R^2 is as defined above;

10 n is an integer of 1-4;

10 R^b is each, independently, hydrogen, halo, hydroxy, mercapto, $(\text{C}_1\text{-C}_4)\text{alkyl}$, $(\text{C}_1\text{-C}_4)\text{alkoxy}$, $(\text{C}_1\text{-C}_4)\text{thioalkyl}$, $(\text{C}_1\text{-C}_4)\text{hydroxyalkyl}$, nitro, cyano, methylenedioxy, ethylenedioxy, COCH_3 , CF_3 , OCF_3 , SCF_3 , COOH , SO_3H , SO_2F , phenyl or phenyl substituted by a group selected from halo, hydroxy, mercapto, $(\text{C}_1\text{-C}_4)\text{alkyl}$, $(\text{C}_1\text{-C}_4)\text{alkoxy}$, $(\text{C}_1\text{-C}_4)\text{thioalkyl}$, $(\text{C}_1\text{-C}_4)\text{hydroxyalkyl}$, amino, nitro, cyano, CF_3 , COOH , SO_3H , $\text{SO}_2\text{NR}^2\text{R}^3$ in which R^2 and R^3 are as defined below, and SO_2F ;

15 R^a is also benzyloxy substituted on the phenyl portion by a group defined above, NR^2R^3 in which R^2 is H or $(\text{C}_1\text{-C}_4)\text{alkyl}$ and R^3 is H, $(\text{C}_1\text{-C}_4)\text{alkyl}$, phenyl or phenyl substituted by a group as defined above;

20 R^1 is $(\text{C}_1\text{-C}_4)\text{alkyl}$, or a pharmaceutically acceptable salt thereof;

20 the quinazoline compounding having a first solubility in water;

20 (b) converting the quinazoline compound to an acid addition salt of the quinazoline compound having a second solubility in water greater than the first solubility in water;

25 (c) combining polyethylene glycol with the acid addition salt of the quinazoline compound to form a first mixture, the first mixture having a third solubility of quinazoline compound in water/polyethylene glycol greater than the second solubility in water;

(d) combining a phospholipid with the first mixture to form a second mixture, the second mixture having a fourth solubility of quinazoline compound in water/polyethylene glycol/phospholipid greater than the third solubility in water/polyethylene glycol.

5

31. The method of claim 30, wherein the second solubility is at least about 50 times greater than the first solubility.

10 32. The method of claim 30, wherein the third solubility is at least about 90 times greater than the first solubility.

33. The method of claim 30, wherein the fourth solubility is at least about 190 times greater than the first solubility.

15 34. The method of claim 30, wherein the quinazoline compound is selected from:
4-(3',5'-dibromo-4'-methylphenyl)amino-6,7-dimethoxyquinazoline,
4-(2',4',6'-tribromophenyl)amino-6,7-dimethoxyquinazoline,
4-(2',3',5',6'-tetrafluoro-4'-bromophenyl)amino-6,7-dimethoxyquinazoline,
4-(4'-fluorophenyl)amino-6,7-dimethoxyquinazoline,
4-(3'-fluorophenyl)amino-6,7-dimethoxyquinazoline,
20 4-(2'-fluorophenyl)amino-6,7-dimethoxyquinazoline,
4-(4'-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,
4-(2'-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,
4-(3',5'-bis-trifluoromethylphenyl)amino-6,7-dimethoxyquinazoline,
4-(3',5'-dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline, and
25 4-(3'-chloro-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline.

35. The method of claim 30, wherein the quinazoline compound is selected from:

4-(3',5'-dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,
4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,
4-(3'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline,
4-(2'-hydroxy-naphthyl-3')-amino-6,7-dimethoxyquinazoline,
5 4-{4'-[2''-(4''-aminophenyl)-hexafluoropropyl]phenyl}-amino-6,7-
dimethoxyquinazoline, and
4-(3'-trifluoromethoxyphenyl)-amino-6,7-dimethoxyquinazoline.

36. The method of claim 30, wherein the phospholipid is an unsaturated
10 phospholipid.

37. The method of claim 30, wherein the phospholipid is an anionic phospholipid.

38. The method of claim 30, wherein the phospholipid is a polyethylene glycol
15 phospholipid.

39. The method of claim 30, wherein the phospholipid is a polyethylene glycol
phosphatidylethanolamine.

20 40. The method of claim 30, wherein the phospholipid is 1,2-dipalmitoyl-sn-glycero-
3-phosphoethanolamine-N-[poly(ethylene glycol)5000].

41. The method of claim 30, wherein the phospholipid is 1,2-dipalmitoyl-sn-glycero-
3-phosphoethanolamine-N-[poly(ethylene glycol)2000].

25

42. A product produced by the method of claim 30.

43. A method comprising, administering to a mammal a formulation comprising:

(a) a phospholipid; and

(b) a mast cell inhibiting amount of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline.

5 44. The method of claim 43, wherein the phospholipid is an unsaturated phospholipid.

45. The method of claim 43, wherein the phospholipid is an anionic phospholipid.

10 46. The method of claim 43, wherein the phospholipid is a polyethylene glycol phospholipid.

47. The method of claim 43, wherein the phospholipid is a polyethylene glycol phosphatidylethanolamine.

15 48. The method of claim 43, wherein the phospholipid is 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethylene glycol)5000].

49. The method of claim 43, wherein the phospholipid is 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethylene glycol)2000].

20

50. The method of claim 43, further comprising a surfactant.

51. The method of claim 43, wherein the surfactant is a block copolymer of ethyleneoxide and propyleneoxide.

25

52. The method of claim 43, further comprising propylene glycol.

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53. The method of claim 43, further comprising:

- (c) a surfactant
- (d) propylene glycol and
- (e) water.

5

54. The method of claim 43, wherein the phospholipid is polyethylene glycol phosphatidylethanolamine and the surfactant is a block copolymer of ethyleneoxide and propyleneoxide.

10 55. The method of claim 43, wherein the phospholipid is an anionic phospholipid and the 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline compound is a chloride salt of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline.

15 56. The method of claim 43, wherein:

- (a) the phospholipid concentration is about 0.2 to 2.5 w/v%;
- (b) the 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline concentration is less than about 0.2 w/v%;
- (c) the surfactant concentration is about 0.05-2 w/v%;
- (d) the propylene glycol concentration is about 5-20 w/v%; and
- (e) the balance is water.

20 57. The method of claim 43, wherein:

- (a) the phospholipid concentration is about 1.84 w/v%;
- (b) the 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline concentration is about 0.2 w/v%;
- (c) the surfactant concentration is about 0.42 w/v%;
- (d) the propylene glycol concentration is about 9.33 w/v%; and
- (e) the water concentration is 88.21.

58. The method of claim 43, wherein the phospholipid and 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline form a micellar formulation with a mean particle size less than about 10 nm.

5

59. The method of claim 53, wherein the phospholipid and 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline form a micellar formulation with a mean particle size less than about 10 nm.

10 60. A method comprising, administering to a mammal a formulation comprising:

- (a) a low hydrophylicity lipophylicity balance portion comprising:
 - (i) a block copolymer of ethylene oxide and propylene oxide;
 - (ii) an ethoxylated castor oil;
 - (iii) propylene glycol;

15 (b) a high hydrophylicity lipophylicity balance portion comprising:

- (i) lecithin;
- (ii) a triglyceride of caprylic acid;

(c) water; and

(d) a mast cell inhibiting amount of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline.

20

61. The method of claim 60, wherein the low hydrophylicity lipophylicity balance portion, the high hydrophylicity lipophylicity balance portion, the water and the mast cell inhibiting amount of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline form a microemulsion with a mean particle size of about 10-25 nm.

25

62. The method of claim 60, wherein the low hydrophylicity lipophylicity balance portion comprises:

- (i) about 2 w/v% of the block copolymer of ethylene oxide and propylene oxide;
- (ii) about 18 w/v% of the ethoxylated castor oil; and
- (iii) about 80 w/v% of the propylene glycol.

5

63. The method of claim 60, wherein the high hydrophylicity lipophylicity balance portion comprises:

- (i) about 40 w/v% of the lecithin; and
- (ii) about 60 w/v% of the triglyceride of caprylic acid.

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64. The method of claim 60, wherein the low hydrophylicity lipophylicity balance portion comprises:

- (i) about 2 w/v% of the block copolymer of ethylene oxide and propylene oxide;
- (ii) about 18 w/v% of the ethoxylated castor oil;
- (iii) about 80 w/v% of the propylene glycol; and

the high hydrophylicity lipophylicity balance portion comprises:

- (i) about 40 w/v% of the lecithin;
- (ii) about 60 w/v% of the triglyceride of caprylic acid;

20 the water and the quinazoline compound form a microemulsion with a mean particle size of about 10-25 nm.

25 65. The method of claim 60, wherein the mast cell inhibiting amount of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline is an acid addition salt of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline.

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